



Machine learning to characterize antimicrobial resistance

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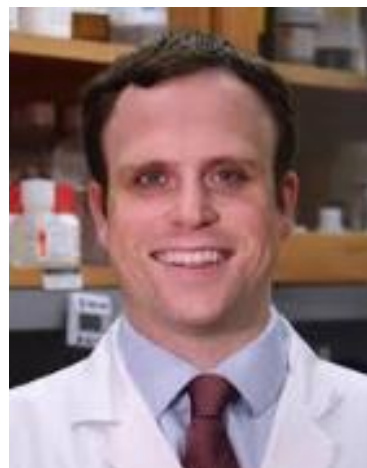


COVID-19 International Research Team

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National Aeronautics and Space
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California Institute of Technology



Nitin K Singh

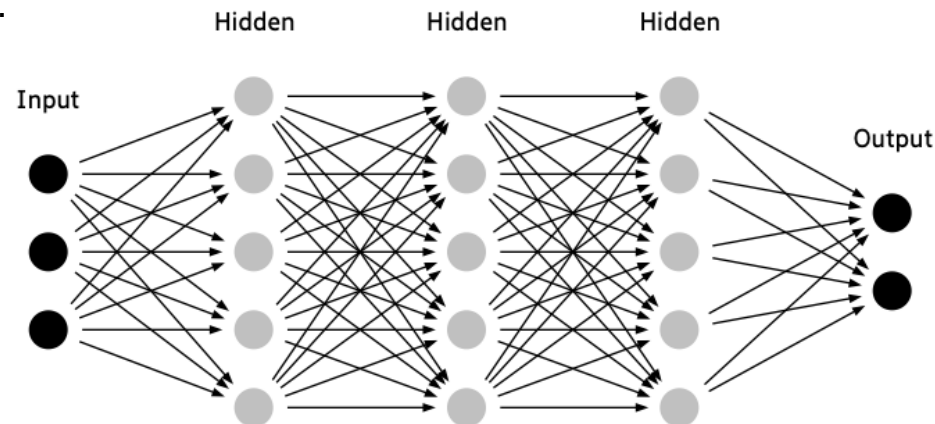


Afshin Beheshti



Supervised Machine Learning for Prediction of Antimicrobial Resistance

- A Deep Learning approach for predicting antibiotic resistance genes (ARGs) from metagenomic data
- Curated database of 14,933 genes from three databases (CARD, ARDB, and UNIPROT)
- Model:
 - Input layer of 4333 units that correspond to the ARGs from ARDB and CARD
 - 4 hidden layers of 2k, 1k, 500 and 100 units
 - Output layer of DNN consists of 30 units that correspond to antibiotic resistance categories (102 antibiotics consolidated into 30 antibiotic categories)
- Two models: SS (short read sequences) and LS (full gene length sequences)
 - The CARD and ARDB genes were selected to represent known ARGs, whereas the UNIPROT genes were used for training and validation of the models.



A simple model of Deep Feedforward Neural Network Structure (dotnets/Graphviz)

DeepARG, Arango-Argoty et al. *Microbiome* (2018)

Antibiotic Resistance Mechanisms

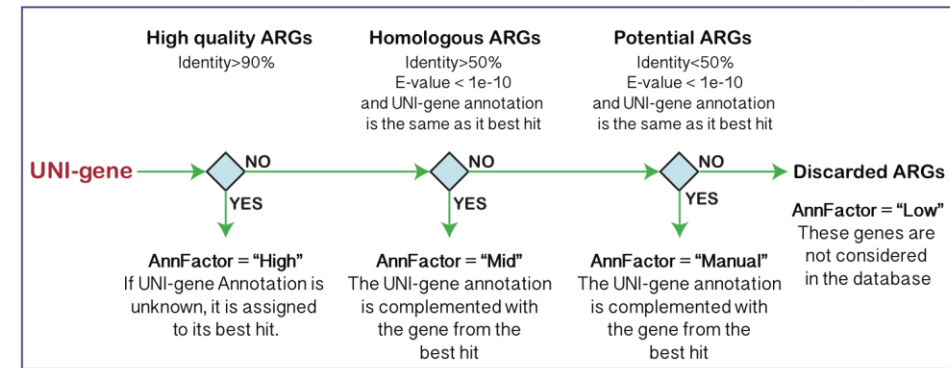
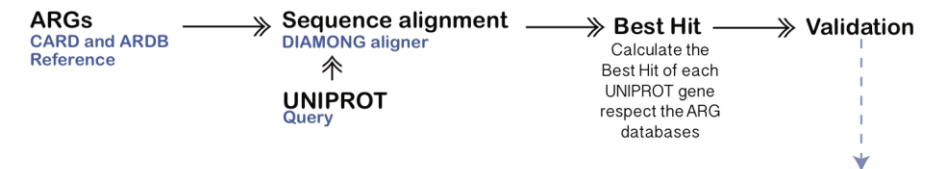
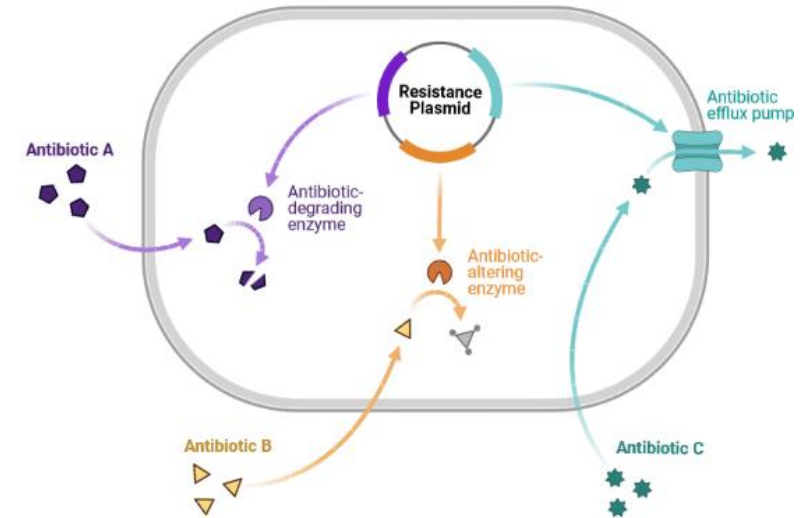
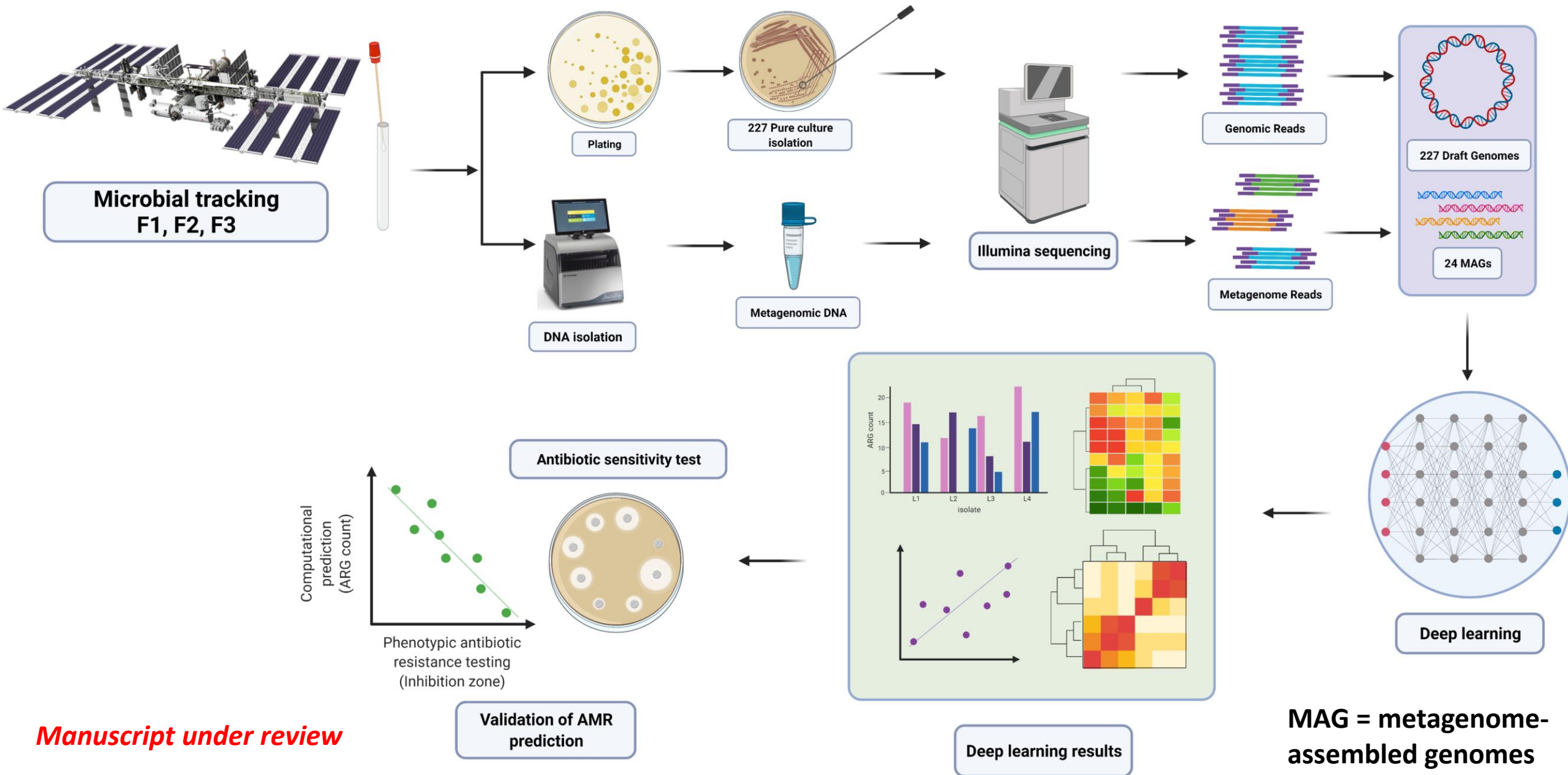


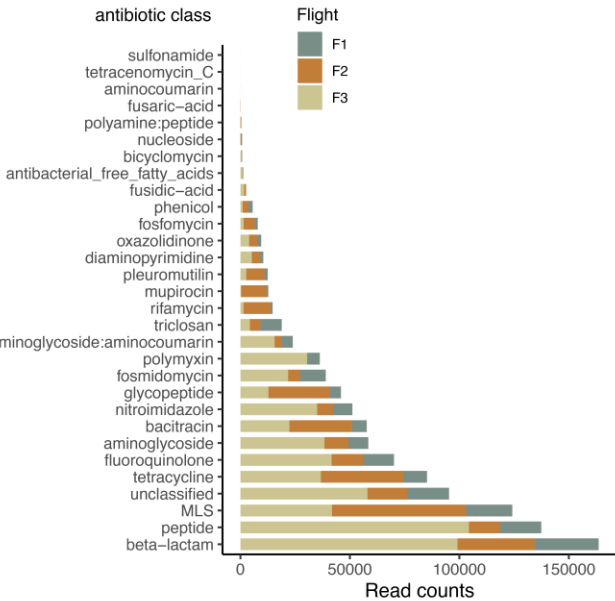
Figure obtained from: <https://bench.cs.vt.edu/deeparg>

Supervised Machine Learning for Prediction of Antimicrobial Resistance



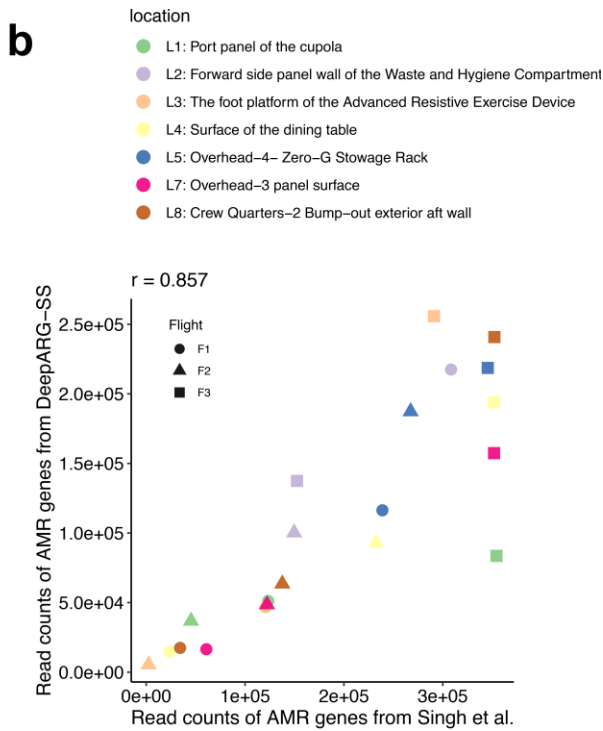
Prediction of Antibiotic Resistance Genes (ARGs) using a pre-trained DeepARG-SS model

a



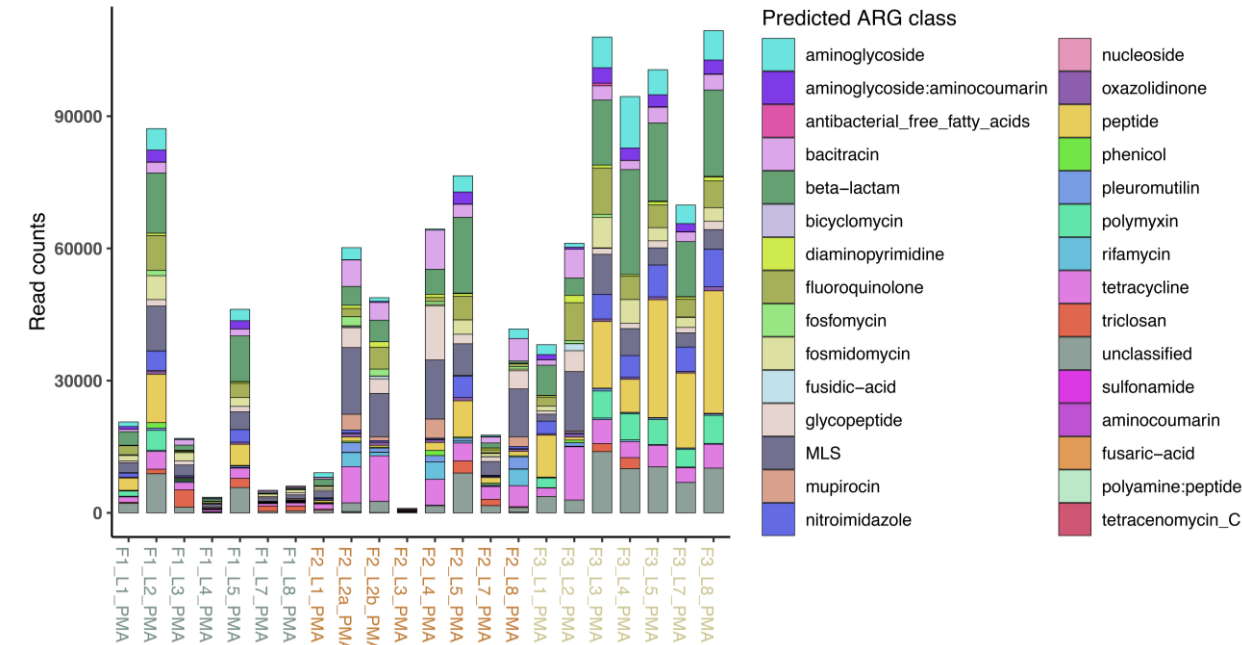
Distribution of ARG read counts across antibiotic classes for the three flights

b



Correlation of read counts found by DeepARG-SS and those in Singh et al. (2018).

c



Read counts of ARG class across flights for each location for propidium monoazide (PMA)-treated samples in Singh et al. (2018)

Propidium monoazide (PMA) is a photoreactive DNA-binding dye that preferentially binds to dsDNA. It is used to detect viable microorganisms by qPCR

Singh et al. Microbiome (2018) 6:204
<https://doi.org/10.1186/s40168-018-0585-2>

Microbiome

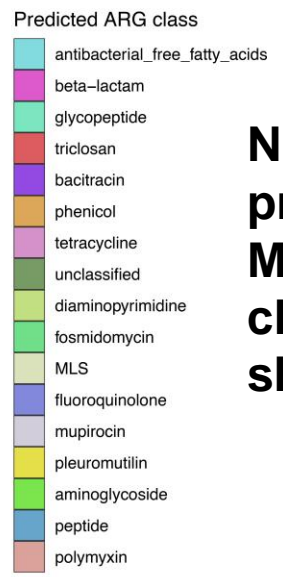
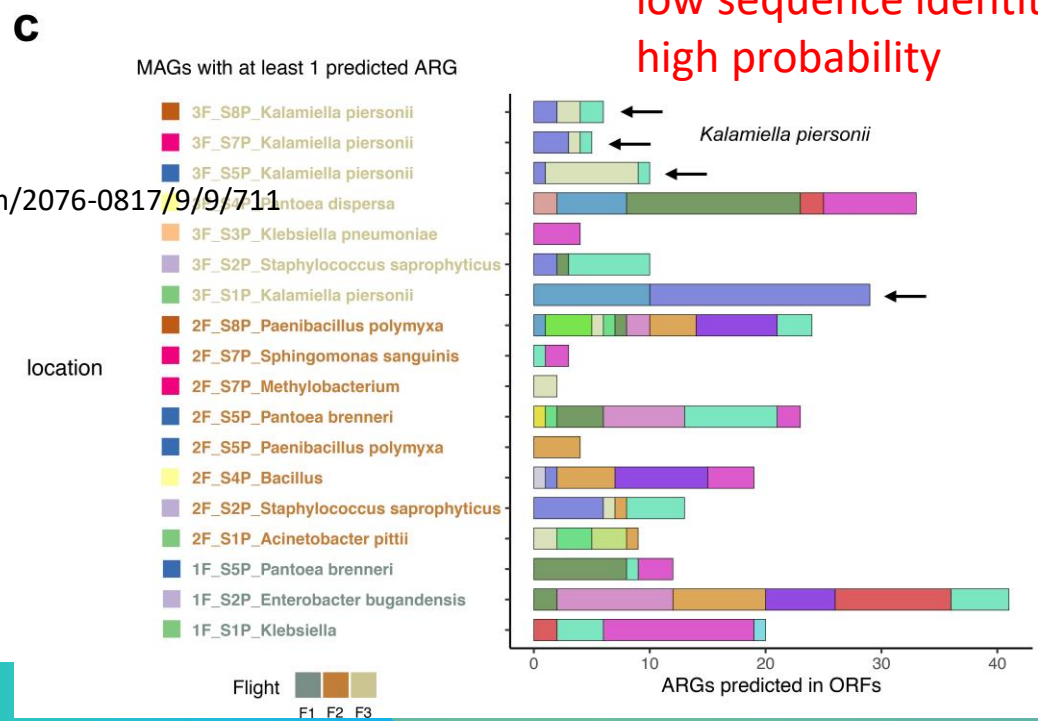
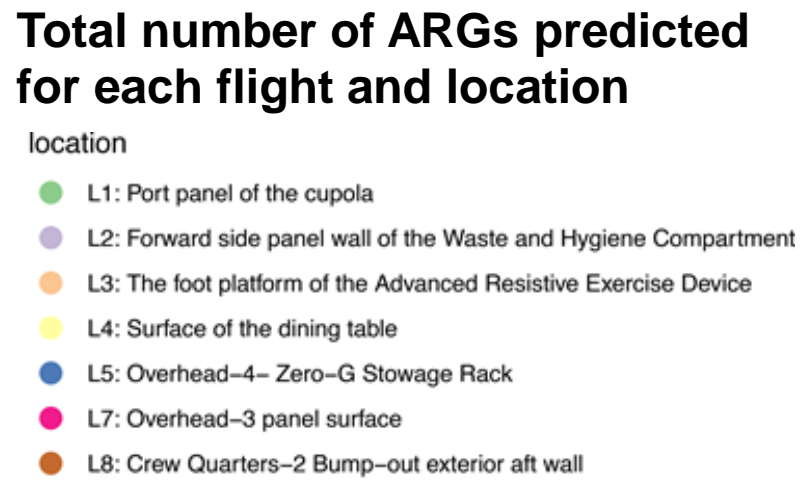
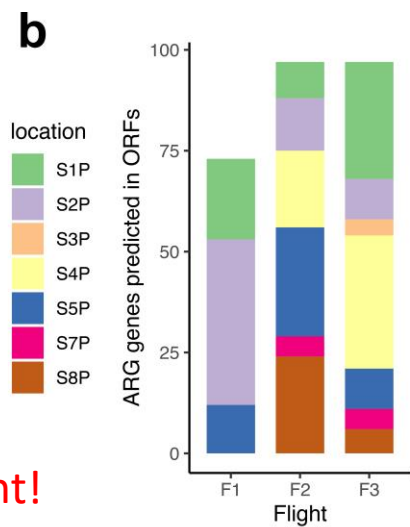
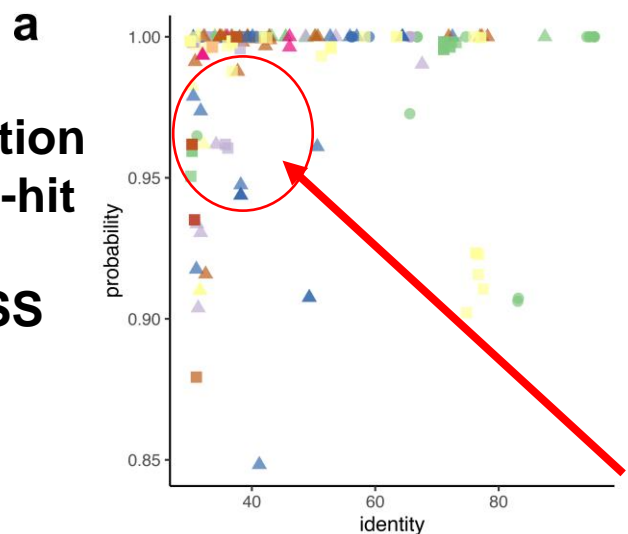
RESEARCH Open Access

Succession and persistence of microbial communities and antimicrobial resistance genes associated with International Space Station environmental surfaces

Nitin Kumar Singh¹, Jason M. Wood¹, Fathi Karouia^{2,3} and Kasthuri Venkateswaran^{1*}

ARGs detected in Open Reading Frames (ORFs) in metagenome-assembled genomes (MAGs) from PMA-treated samples

Distribution of DeepARG classification probability and best-hit identity in MAGs retrieved from the ISS

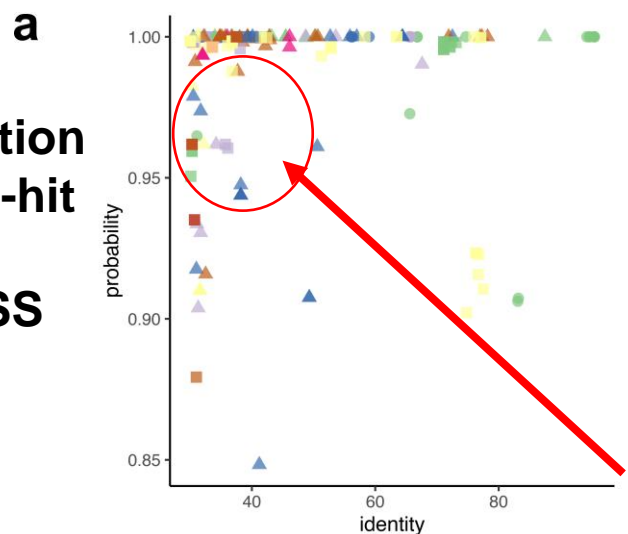


Number of ARGs predicted for each MAG. Most common antibiotic class (*multi-drug*) not shown

Manuscript under review

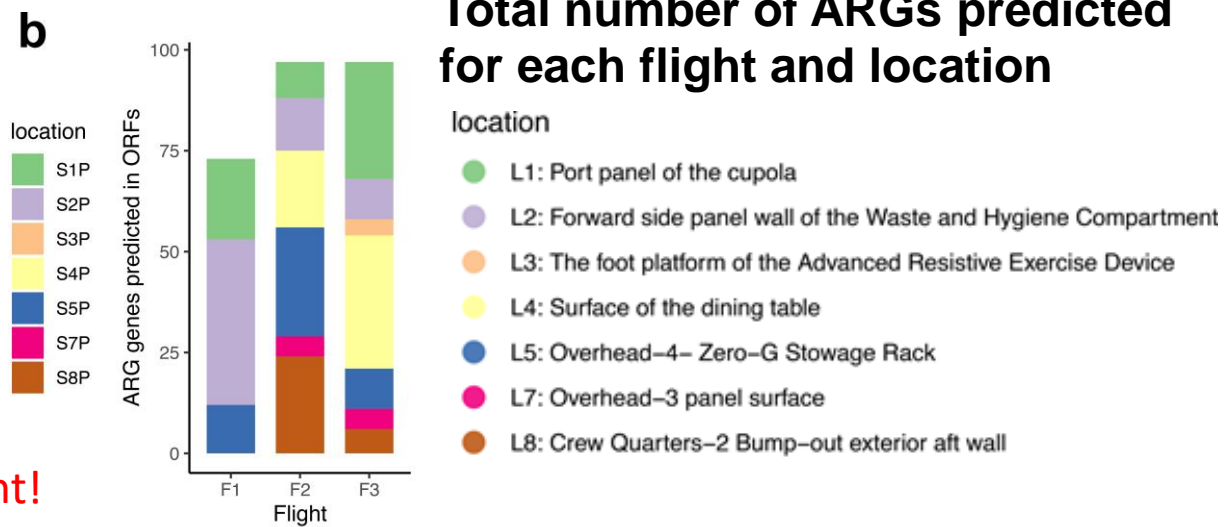
ARGs detected in Open Reading Frames (ORFs) in metagenome-assembled genomes (MAGs) from PMA-treated samples

Distribution of DeepARG classification probability and best-hit identity in MAGs retrieved from the ISS



Important!
low sequence identity (mostly discarded by traditional approaches) but high probability

Total number of ARGs predicted for each flight and location



pathogens

<https://www.mdpi.com/2076-0817/9/9/711>

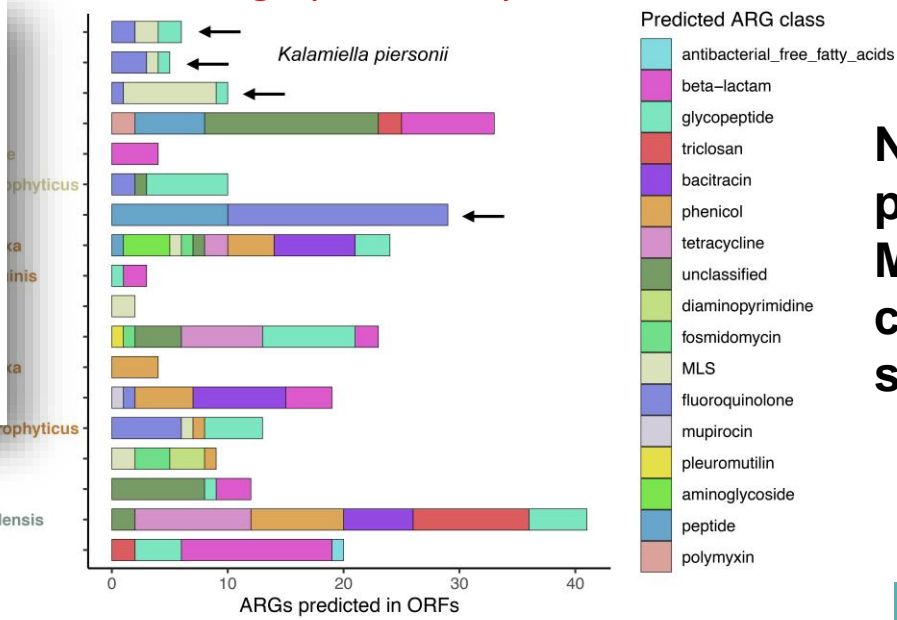
Article

First Report of Pathogenic Bacterium *Kalamiella piersonii* Isolated from Urine of a Kidney Stone Patient: Draft Genome and Evidence for Role in Struvite Crystallization

Punchappady Devasya Rekha ^{1,*}, Asif Hameed ^{1,2,†}, Muhammed A. P. Manzoor ^{1,†}, Mangesh V. Suryavanshi ^{1,†}, Sudeep D. Ghate ¹, A. B. Arun ¹, Sneha S. Rao ^{1,†}, Athmika ^{1,†}, Sukesh Kumar Bajire ¹, M. Mujeerurrahiman ³ and C.-C. Young ²

2F_S2P_Staphylococcus saprophyticus
2F_S1P_Acinetobacter pittii
1F_S5P_Pantoea brenneri
1F_S2P_Enterobacter bugandensis
1F_S1P_Klebsiella

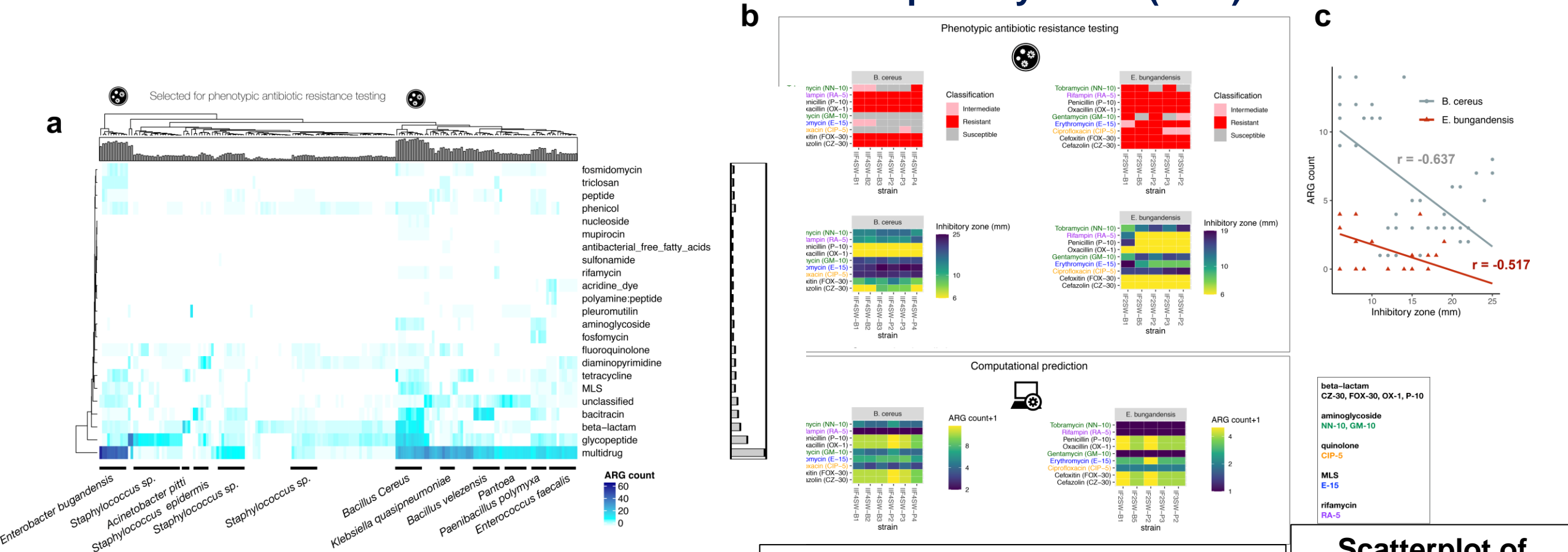
Flight F1 F2 F3



Number of ARGs predicted for each MAG. Most common antibiotic class (*multi-drug*) not shown

Manuscript under review

Heatmap and clustering of ARG counts detected in Microbial Tracking-1 pure strains isolated from the ISS and Antibacterial Susceptibility Tests (AST) validations



Heatmap with ARG count. The barplots illustrate the number of ARGs across rows and across columns.

Manuscript under review

Antibacterial Susceptibility Tests (AST) on *E. bugandensis* and *B. cereus* strains for several antibiotics (top), and comparison with machine learning predictions shown in (a)

Scatterplot of zone of inhibition value (in mm.) and ARG count shown in (b), together with a linear model fit.

Heatmap and clustering of ARG counts detected in Microbial Tracking-1 pure strains isolated from the ISS and Antibacterial Susceptibility Tests (AST) validations

SCIENTIFIC REPORTS

<https://www.nature.com/articles/s41598-018-23069-z.pdf>

OPEN

Enterobacter bugandensis: a novel enterobacterial species associated with severe clinical infection

Niladri Bhusan Pati¹, Swapnil Prakash Doijad², Tilman Schultze¹, Gopala Krishna Mannala¹, Yancheng Yao¹, Sangeeta Jaiswal², Daniel Ryan², Mrutyunjay Suar², Konrad Gwozdziński¹, Boyke Bunk³, Mobarak Abu Mraheil¹, Mohamed A. Marahiel¹, Julian D. Hegemann¹, Cathrin Spröer³, Alexander Goesmann², Linda Falgenhauer¹, Torsten Hain¹, Can Imirzalioglu¹, Stephen E. Mshana⁶, Jörg Overmann³ & Trinad Chakraborty¹

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[https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247\(21\)00098-7/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00098-7/fulltext)

ARTICLES | VOLUME 2, ISSUE 10, E536-E544, OCTOBER 01, 2021

Uncovering the novel *Enterobacter cloacae* complex species responsible for septic shock deaths in newborns: a cohort study

Delphine Girlich, PhD[†] • Souad Ouzani, PharmD[†] • Cécile Emeraud, PharmD • Lauraine Gauthier, PharmD

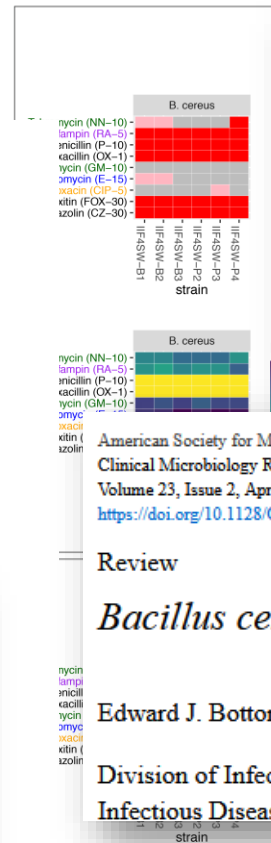
Rémy A Bonnin, PhD • N Le Sache, MD • et al. Show all authors • Show footnotes

Open Access • Published: July 23, 2021 • DOI: [https://doi.org/10.1016/S2666-5247\(21\)00098-7](https://doi.org/10.1016/S2666-5247(21)00098-7)



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b



frontiers
in Microbiology

published: 19 August 2020
doi: 10.3389/fmicb.2020.01731

<https://www.frontiersin.org/articles/10.3389/fmicb.2020.01731/full>

You Can't *B. cereus* – A Review of *Bacillus cereus* Strains That Cause Anthrax-Like Disease

Victoria M. Baldwin*

Distill, Salisbury, United Kingdom

American Society for Microbiology
Clinical Microbiology Reviews
Volume 23, Issue 2, April 2010, Pages 382-398
<https://doi.org/10.1128/CMR.00073-09>

Review <https://journals.asm.org/doi/epub/10.1128/CMR.00073-09>

Bacillus cereus, a Volatile Human Pathogen

Edward J. Bottone*

Division of Infectious Diseases, Mount Sinai School of Medicine, New York, New York, and Division of Infectious Diseases, New York Medical College, Valhalla, New York

Antibacterial Susceptibility Tests (AST) on *E. bugandensis* and *B. cereus* strains for several antibiotics (top), and comparison with machine learning predictions shown in (a)

Scatterplot of zone of inhibition value (in mm.) and ARG count shown in (b), together with a linear model fit.

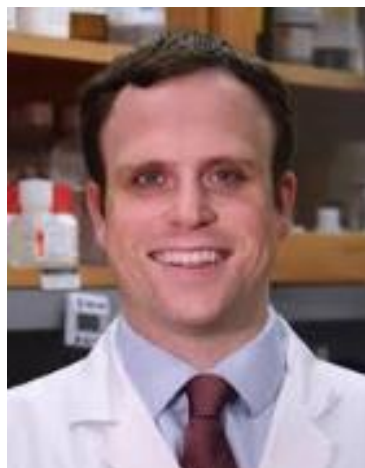
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